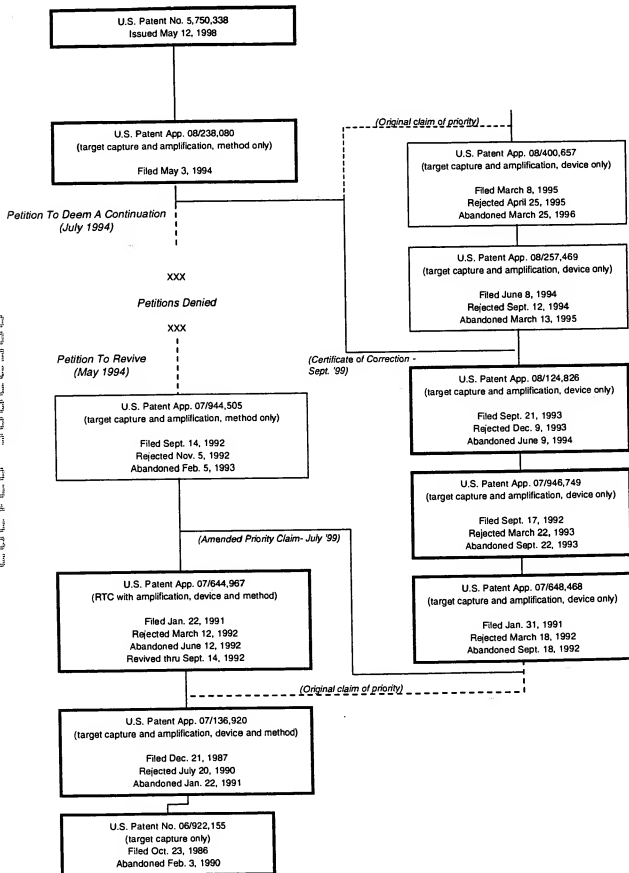


09533906-021202

# '338 PATENT HISTORY WITH POST-ISSUANCE CORRECTIONS AND AMENDMENTS



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20 Attorneys for Plaintiff  
21 Gen-Probe Incorporated

22 UNITED STATES DISTRICT COURT  
23 SOUTHERN DISTRICT OF CALIFORNIA

24 GEN-PROBE INCORPORATED,

25 Plaintiff,

26 v.

27 VYSIS, INC.,

28 Defendant.

No. 99-CV-2668H AJB  
JUDGE MARILYN L. HUFF

**REPLY DECLARATION OF STEPHEN P.  
SWINTON IN SUPPORT OF GEN-PROBE'S  
MOTION FOR PARTIAL SUMMARY JUDGMENT**

Date: June 8, 2001  
Time: 10:30 a.m.  
Dept: Courtroom 1

29 I, Stephen P. Swinton, declare as follows:

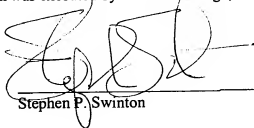
30 1. I am a member of the State Bar of California and admitted to practice before this  
31 Court. I am a partner with the law firm of Cooley Godward LLP and am one of the counsel of

1 record in this action for plaintiff Gen-Probe Incorporated.

2 2. I attended the deposition of Walter King, Ph.D., at Downers Grove, Illinois on  
3 April 18, 2001. I asked the questions and heard the responses given by Dr. Lawrie at the  
4 deposition. The deposition of Dr. King was stenographically recorded and transcribed. The  
5 excerpts of the Lawrie deposition set forth in Exhibit 17 to the accompanying Reply Notice of  
6 Lodgment are true and correct copies of the certified deposition transcript and accurately state the  
7 questions and answers at the King deposition.

8 3. I attended the deposition of Donald Neil Halbert, at Abbot, Illinois on April 19,  
9 2001. I asked the questions and heard the responses given by Dr. Halbert at the deposition. The  
10 deposition of Dr. Halbert was stenographically recorded and transcribed. The excerpts of the  
11 Halbert deposition set forth in Exhibit 18 to the accompanying Reply Notice of Lodgment are true  
12 and correct copies of the certified deposition transcript and accurately state the questions and  
13 answers at the Halbert deposition.

14 I declare under penalty of perjury under the laws of the United States of America that all  
15 statements made herein of my own knowledge are true and that all statements made on information  
16 and belief are believed to be true. This declaration was executed by me at San Diego, California  
17 on May 31, 2001.

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Stephen P. Swinton

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Attorneys for Plaintiff  
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UNITED STATES DISTRICT COURT  
SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE INCORPORATED,

Plaintiff,

v.

VYSIS, INC.,

Defendant.

No. 99CV2668 H (AJB)  
THE HONORABLE MARILYN L. HUFF

**REPLY DECLARATION OF R. WILLIAM BOWEN  
IN SUPPORT OF GEN-PROBE'S MOTION FOR  
SUMMARY JUDGMENT**

Date: June 8, 2001  
Time: 10:30 a.m.  
Place: Courtroom 1

I, R. William Bowen, declare as follows:

1. I am a member of the State Bar of California and admitted to practice before this Court. I am one of the counsel of record in this action for plaintiff Gen-Probe Incorporated.
2. I attended the deposition of Anthony J. Janiuk, Esq. at Boston, Massachusetts on May 16, 2001. I asked the questions and heard the responses given by Mr. Janiuk at the deposition. The deposition of Mr. Janiuk was stenographically recorded and transcribed. The

1 excerpts of the Janiuk deposition set forth in Exhibit 13 to the accompanying reply notice of  
2 lodgment are true and correct copies of the certified deposition transcript and accurately state the  
3 questions and answers at the Janiuk deposition.

4 3. At the deposition of Mr. Janiuk, a letter dated November 14, 1989 from Mr. Janiuk  
5 to Dr. James Richards was marked as Plaintiff's Deposition Exhibit 143 and authenticated by the  
6 witness. A true and correct copy of this letter is attached as Exhibit 11 to the accompanying reply  
7 notice of lodgment.

8 4. I attended the deposition of Alan E. Smith, Ph.D., at Cambridge, Massachusetts on  
9 May 17, 2001. I asked the questions and heard the responses given by Dr. Smith at the deposition.  
10 The deposition of Dr. Smith was stenographically recorded and transcribed. The excerpts of the  
11 Smith deposition set forth in Exhibit 14 to the accompanying reply notice of lodgment are true and  
12 correct copies of the certified deposition transcript and accurately state the questions and answers  
13 at the Smith deposition.

14 5. I attended the deposition of David Ward, Ph.D., at New Haven, Connecticut on  
15 May 18, 2001. I asked the questions and heard the responses given by Dr. Ward at the deposition.  
16 The deposition of Dr. Ward was stenographically recorded and transcribed. The excerpts of the  
17 Ward deposition set forth in Exhibit 15 to the accompanying reply notice of lodgment are true and  
18 correct copies from the preliminary or "rough" deposition transcript and accurately state the  
19 questions and answers at the Ward deposition.

20 6. I attended the deposition of Jon Lawrie, Ph.D., at Raleigh - Durham, North Carolina  
21 on February 15, 2001. I asked the questions and heard the responses given by Dr. Lawrie at the  
22 deposition. The deposition of Dr. Lawrie was stenographically recorded and transcribed. The  
23 excerpts of the Lawrie deposition set forth in Exhibit 16 to the accompanying reply notice of  
24 lodgment are true and correct copies of the certified deposition transcript and accurately state the  
25 questions and answers at the Lawrie deposition.

26 7. At the deposition of Dr. Lawrie, a set of handwritten notes made by Dr. Lawrie was  
27 marked as Plaintiff's Deposition Exhibit 49 and authenticated by the witness. A true and correct  
28 copy of page these notes is attached as Exhibit 12 to the accompanying reply notice of lodgment.

1 I hereby declare under penalty of perjury that all statements made herein of my own  
2 knowledge are true and that all statements made on information and belief are believed to be true.

3 Executed at San Diego, California on May 31, 2001.

4 R. William Bowen  
5 R. William Bowen  
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12 Attorneys for Plaintiff  
Gen-Probe Incorporated

13 UNITED STATES DISTRICT COURT  
14 SOUTHERN DISTRICT OF CALIFORNIA  
15

16  
17 GEN-PROBE INCORPORATED,

18 Plaintiff,

19 v.

20 VYSIS, INC.,

21 Defendant.  
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No. 99-CV-2668H AJB  
JUDGE MARILYN L. HUFF

REPLY DECLARATION OF DR. JOSEPH O.  
FALKINHAM IN SUPPORT OF GEN-PROBE'S  
MOTION FOR PARTIAL SUMMARY JUDGMENT

Date: June 8, 2001  
Time: 10:30 a.m.  
Dept.: Courtroom 1

1 I, Joseph O. Falkinham, III, hereby declare as follows:

2 1. I have personal knowledge of the facts set forth below, and, if called as a witness in  
3 this action, I could and would testify competently to the truth thereof.

4 2. I have been retained as an expert witness in this lawsuit. I have reviewed the  
5 specification and claims of the '338 patent), as well as Vysis, Inc.'s Opposition to Gen-Probe's  
6 Motion for Summary Judgment and the Declaration of Dr. David H. Persing. I submit this  
7 declaration to rebut certain statements made by Dr. Persing.

8 SUMMARY OF OPINION

9 3. In paragraph 13 of his declaration, Dr. Persing states that he believes that Example  
10 5 describes specific amplification because:

11 "In particular, while Example 5 states initially that random  
12 oligohexamer primers can be used to achieve non-specific  
13 amplification, Example 5 also discloses that "[a]lternatively, the  
14 double stranded DNA can be formed by synthesis starting from  
15 capture probe a." Col. 31, lines 48-49. In this instance, the capture  
16 probe acts as the primer. Since the capture probe binds specifically  
17 to the target DNA, the capture probe would be a specific primer to  
18 the target. This is an example of specific amplification because the  
19 primer, capture probe a, binds to a specific, unique DNA sequence in  
20 the target organism."

21 4. I disagree with Dr. Persing's conclusion for the following reasons.

22 5. Example 5 of the '338 specification teaches only the combination of target capture  
23 with *non-specific* amplification. Example 5 is set forth in three paragraphs of text beginning at col.  
24 31, line 24 of the '338 patent. The first paragraph consists of a single sentence that states that the  
25 example teaches non-specific amplification:

26 In this example, both *non-specific* replication of target DNA and  
27 transcription of that DNA are used to amplify capture target DNA.  
28 (Exh. 8, at col. 31, ll. 24-54, emphasis added.) The second paragraph of example 5 provides the  
29 details of a particular method, and teaches the use of *random* (e.g., non-specific) primers and non-  
30 specific transcription in the amplification process used in the method. (Exh. 8, at col. 31, ll.  
31 31-33.) As a result of these explicit statements, it is my opinion that a person skilled in the art  
32 would understand that Example 5 discloses a non-specific method of amplification.

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6. This understanding is reinforced by the fact that Example 5 refers to and incorporates Figure 5 of the drawings included in the patent. (Exhibit 8 at col. 31, l. 28.) The drawings, including Figure 5, are discussed and described in the text of the patent specification:

In Step 3 of FIGS. 4, 5 and 6, the isolated target is *non-specifically* amplified to form a multitude of amplification products.

(*Id.* at col. 15, ll. 56-58, emphasis added.) Thus, Dr. Persing's contention that Example 5 teaches specific amplification is contrary to the description of the Figure associated with Example 5.

7. Further, use of the capture probe as a primer in Example 5 of the '338 Patent does not disclose amplification with specific primers. The addition of DNA polymerase and nucleoside-triphosphates would simply result in the extension of the capture probe DNA molecule by synthesis of a complement to the sequence of the target DNA not hydrogen-bonded to the capture probe. This extension would occur only once. Extension of the capture probe is not amplification of the target sequence. Because only a complement of the target would be synthesized, there is no amplification of the target sequence. It is also not clear from Example 5 that even extension of the capture probe using the target DNA as template would occur. If the capture probe was bound to the matrix through the 3' terminus such that its 5' end was free, there could be no extension. DNA polymerases require a '3-OH end to initiate extension.

8. One of ordinary skill would recognize that the nucleic acid extension in Example 5 would not be amplification, which is exponential and involves repeated steps. Using the target DNA as template would result in a one time, linear extension of the capture probe. The absence of a second specific probe means that there would be no amplification or further replication of the double-stranded DNA resulting from the DNA polymerase-catalyzed extension of the capture probe.

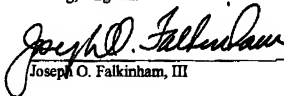
9. Dr. Persing's conclusion that Example 5 discloses specific amplification is incorrect because it is based on the incorrect assumption that the capture probe described in Example 5 "binds specifically to the target DNA." There is nothing in the 338 'patent that describes this capture probe as one that "binds specifically to the target DNA." Rather, Example 5 says that "denatured sample DNA is captured as described above". "Above" is Example 4, which simply

1 states that "A recA protein coated capture probe is then added to the digested target DNA . . . . The  
2 recA protein coated probe contains a nucleic acid sequence (a) that is homologous to a first target  
3 (a') sequence of the target DNA, as well as a homopolymer sequence on a capture bead." These  
4 passages do not state that the capture probe is specific to the target DNA. The fact that a probe is  
5 "homologous" does not mean that the probe is specific. "Homologous" has a very specific  
6 meaning in the art. Two sequences are "homologous" if one evolved from the other.  
7 "Homologous" does not mean that the two sequences are complementary over their entire lengths.

8 10. Even if the '338 specification contained a description of a specific capture probe  
9 which could be used as a primer (which it does not), then the result, as in paragraph 7, would be  
10 extension, not amplification. Further, even a very specific capture probe would likely function  
11 non-specifically as a primer under the very different reaction conditions of the processes of capture  
12 and extension. For example, the conditions necessary for extension would promote non-specific  
13 binding of the capture probe with the target DNA. Thus, the extension would be non-specific.

14 11. I have read Dr. Persing's comments regarding the prosecution history. These  
15 comments do not change any of the opinions that I expressed in my original report or in this report.

16 I hereby declare under penalty of perjury under the laws of the United States of America  
17 and the State of California that all statements made herein of my own knowledge are true and that  
18 all statements made on information and belief are believed to be true. As discovery in this case is  
19 now just beginning, I reserve the right to change or supplement my opinion. This declaration was  
20 executed by me on this 1st day of June, 2001 at Blacksburg, Virginia.

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22 Joseph O. Falkinham, III  
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20 Attorneys for Plaintiff  
21 GEN-PROBE INCORPORATED

22 UNITED STATES DISTRICT COURT  
23 SOUTHERN DISTRICT OF CALIFORNIA

24 GEN-PROBE INCORPORATED,

25 Plaintiff,

26 v.

27 VYSIS, INC.,

28 Defendant.

No. 99CV2668 H (AJB)  
THE HONORABLE MARILYN L. HUFF

**REPLY DECLARATION OF CHRISTINE  
GRITZMACHER IN SUPPORT OF GEN-PROBE'S  
MOTION FOR PARTIAL SUMMARY JUDGMENT**

Date: June 8, 2001  
Time: 10:30 a.m.  
Dept.: Courtroom 1

29 I, Christine Gritzmacher, declare as follows:

30 1. I am a member of the State Bar of California and admitted to practice before the  
31 United States Patent and Trademark Office.

32 2. I am employed as Patent Counsel by Gen-Probe Incorporated and I make this  
33 declaration in support of Gen-Probe's Motion for Partial Summary Judgment.

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3. Gen-Probe has obtained copies of the files of the United States Patent and Trademark Office concerning United States Patent No. 5,750,338 and United States Patent No. 5,714,380.

4. I reviewed the files referred to in paragraph 3. This declaration is based on that review. This declaration is prepared and offered pursuant to Rule 1006 of the Federal Rules of Evidence. The complete patent prosecution files are voluminous and cannot conveniently be examined in court in connection with Gen-Probe's Motion for Summary Judgment. I believe that copies of the individual patent documents referred to in this declaration have been previously submitted by the parties or are submitted as exhibits to accompanying reply notice of lodgment.

5. Vysis' first patent application claiming the combination of target capture and amplification was filed on December 21, 1987. (Vysis Exhibit A.) The claims of this application were rejected by Examiner Chambers. (Vysis Exhibit B.)

6. Vysis filed a "continuation" patent application on January 22, 1991 and the claims of that second application were also rejected by Examiner Chambers. (Vysis Exhibit C.)

7. Vysis filed yet another continuation application on September 14, 1992, leading to a third rejection by the same examiner in November 1992. (Vysis Exhibit D.) Because Vysis did not respond to the November 1992 rejection, the third patent application was abandoned as of February 5, 1993. (Exhibit 19 to Gen-Probe's Reply Notice of Lodgment.)

8. Vysis did not take any further steps to seek a patent for the invention of U.S. patent number 5,750,338 until May 3, 1994, more than one year after it abandoned its third application. In May 1994, Vysis petitioned the PTO to "revive" its third patent application. (Exhibit 20 to Gen-Probe's Reply Notice of Lodgment.) That petition was denied by the PTO on the ground Vysis had waited more than one year after abandonment to seek revival. (Exhibit 21 to Gen-Probe's Reply Notice of Lodgment.)

9. In May 1994, Vysis filed a *fourth* application, an identical copy of the three prior applications. While the prior three applications had all been assigned to the same patent examiner, the fourth application was assigned to a different examiner. On December 5, 1995, in prosecution of this fourth application, Vysis first suggested that the application encompassed methods of

1 specific amplification such as PCR. (Vysis Exhibit E.) That is, Vysis made this statement almost  
2 8 years after the first patent application was filed.

3 10. Exhibit 22 to Gen-Probe's Reply Notice of Lodgment is a summary of the  
4 prosecution history of the '338 patent. I believe Exhibit 22 is an accurate summary of the  
5 information presented therein with respect to the prosecution history. This summary is prepared  
6 and offered pursuant to Rule 1006 of the Federal Rules of Evidence.

7 11. As used in this declaration, the term "Vysis" is used to refer collectively to the  
8 current patent owner, defendant Vysis, Inc., and to all of its predecessors in interest. The term  
9 "Vysis" includes Vysis' parent and predecessor in interest, BP Amoco Corporation.

10 I declare under penalty of perjury under the laws of the United States of America that the  
11 foregoing is true and correct.

12 Executed at San Diego, California on June 1, 2000.

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14 Christine Gritzmacher  
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